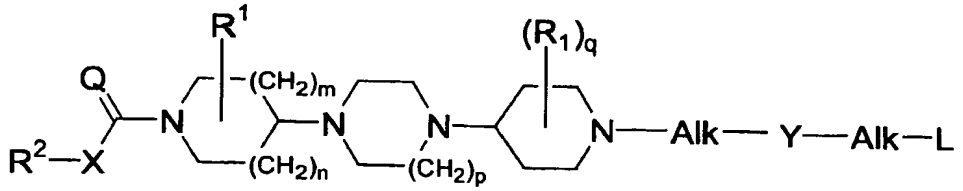
Claims

1. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredients, an opioid analgesic and a therapeutically effective amount of a compound according to Formula (I)



(I)

the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof and prodrugs thereof, wherein :

n is an integer, equal to 0, 1 or 2 ;

m is an integer, equal to 1 or 2, provided that if m is 2, then n is 1 ;

p is an integer equal to 1 or 2 ;

Q is O or NR^3 ;

X is a covalent bond or a bivalent radical of formula -O-, -S- or $-NR^3-$;

each R^3 independently from each other, is hydrogen or alkyl ;

each R^1 independently from each other, is selected from the group of Ar^1, Ar^1-alkyl and di(Ar^1)-alkyl ;

q is an integer equal to 0 or 1 ;

R^2 is alkyl, Ar^2, Ar^2-alkyl, Het^1 or Het^1-alkyl ;

Y is a covalent bond or a bivalent radical of formula -C(=O)- or $-SO_2-$;

each Alk represents, independently from each other, a covalent bond; a bivalent straight or branched, saturated or unsaturated hydrocarbon radical having from 1 to 6 carbon atoms ; or a cyclic saturated or unsaturated hydrocarbon radical having from 3 to 6 carbon atoms ; each radical optionally substituted on one or more carbon atoms with one or more alkyl, phenyl, halo, cyano, hydroxy, formyl and amino radicals ;

L is selected from the group of hydrogen, alkyloxy, Ar^3-oxy, alkyloxycarbonyl, mono- and di(alkyl)amino, mono-and di(Ar^3)amino, Ar^3, Ar^3-carbonyl, Het^2 and Het^2-carbonyl;

Ar^1 is phenyl, optionally substituted with 1, 2 or 3 substituents each independently from each other selected from the group of halo, alkyl, cyano, aminocarbonyl and alkyloxy ;

Ar^2	is naphthalenyl or phenyl, each optionally substituted with 1, 2 or 3 substituents, each independently from each other, selected from the group of halo, nitro, amino, mono- and di(alkyl)amino, cyano, alkyl, hydroxy, alkyloxy, carboxyl, alkyloxycarbonyl, aminocarbonyl and mono- and di(alkyl)aminocarbonyl ;
Ar^3	is naphthalenyl or phenyl, optionally substituted with 1, 2 or 3 substituents each independently from each other selected from the group of alkyloxy, alkyl, halo, hydroxy, pyridinyl, morpholinyl, pyrrolidinyl, imidazo[1,2-*a*]pyridinyl, morpholinylcarbonyl, pyrrolidinylcarbonyl, amino and cyano;
Het^1	is a monocyclic heterocyclic radical selected from the group of pyrrolyl, pyrazolyl, imidazolyl, furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyrazinyl and pyridazinyl ; or a bicyclic heterocyclic radical selected from the group of quinolinyl, quinoxalinyl, indolyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, benzofuranyl and benzothienyl ; each monocyclic and bicyclic heterocyclic radical may optionally be substituted on any atom by a radical selected from the group of halo and alkyl ;
Het^2	is a monocyclic heterocyclic radical selected from the group of pyrrolidinyl, dioxolyl, imidazolidinyl, pyrrazolidinyl, piperidinyl, morpholinyl, dithianyl, thiomorpholinyl, piperazinyl, imidazolidinyl, tetrahydrofuranyl, 2H-pyrrolyl, pyrrolinyl, imidazolinyl, pyrrazolinyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, thiadiazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl and triazinyl ; or a bicyclic heterocyclic radical selected from the group of benzopiperidinyl, quinolinyl, quinoxalinyl, indolyl, isoindolyl, chromenyl, benzimidazolyl, imidazo [1,2-*a*]pyridinyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, benzofuranyl and benzothienyl ; each monocyclic and bicyclic radical optionally substituted with one or more radicals selected from the group of Ar^1, Ar^1alkyl, halo, hydroxy, alkyl, piperidinyl, pyrrolyl, thienyl, oxo, alkyloxy, alkyloxyalkyl and alkyloxycarbonyl ; and
alkyl	is a straight or branched saturated hydrocarbon radical having from 1 to 6 carbon atoms or a cyclic saturated hydrocarbon radical having from 3 to 6 carbon atoms ; optionally substituted on one or more

carbon atoms with one or more radicals selected from the group of phenyl, halo, cyano, oxo, hydroxy, formyl and amino radicals.

2. A pharmaceutical composition according to claim 1, characterized in that

n is 1 ;

m is 1 ;

p is 1 ;

Q is O ;

X is a covalent bond ;

each R^1 is Ar^1 or Ar^1-alkyl ;

q is 0 or 1 ;

R^2 is Ar^2 ;

Y is a covalent bond or a bivalent radical of formula -C(=O)- or -SO_2- ;

each Alk represents, independently from each other, a covalent bond; a bivalent straight or branched, saturated or unsaturated hydrocarbon radical having from 1 to 6 carbon atoms ; or a cyclic saturated or unsaturated hydrocarbon radical having from 3 to 6 carbon atoms ; each radical optionally substituted on one or more carbon atoms with one or more phenyl, halo, cyano, hydroxy, formyl and amino radicals ;

L is selected from the group of hydrogen, alkyloxy, Ar^3-oxy, alkyloxycarbonyl, mono- and di(alkyl)amino, mono-and di(Ar^3)amino, Ar^3 and Het^2;

Ar^1 is phenyl, optionally substituted with 1, 2 or 3 alkyl radicals ;

Ar^2 is phenyl, optionally substituted with 1, 2 or 3 alkyl radicals ;

Ar^3 is phenyl, optionally substituted with 1, 2 or 3 substituents each independently from each other selected from the group of alkyloxy, alkyl, halo, hydroxy, pyridinyl, morpholinyl, pyrrolidinyl, imidazo [1,2-*a*]pyridinyl, morpholinylcarbonyl, pyrrolidinylcarbonyl, amino and cyano ;

Het^2 is a monocyclic heterocyclic radical selected from the group of pyrrolidinyl, piperidinyl, morpholinyl, pyrrolyl, imidazolyl, pyrazolyl, furanyl, thienyl, isoxazolyl, thiazolyl, thiadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl ; or a bicyclic heterocyclic radical selected from the group of benzopiperidinyl, quinolinyl, quinoxalinyl, indolyl, chromenyl and benzimidazolyl ; each monocyclic and bicyclic radical optionally substituted with one or more radicals selected from the group of Ar^1, Ar^1alkyl, halo, hydroxy, alkyl, piperidinyl, pyrrolyl, thienyl, oxo and alkyloxycarbonyl ; and

alkyl is a straight hydrocarbon radical having 1 to 6 carbon atoms, optionally substituted with one or more halo radicals .

3. A pharmaceutical composition according to any one of claims 1 to 2, characterized in that R^1 is Ar^1methyl and attached to the 2-position or R^1 is Ar^1 and attached to the 3-position.

4. A pharmaceutical composition according to any one of claims 1 to 3, characterized in that the R^2-X-C(=Q)- moiety is 3,5-di-(trifluoromethyl) phenylcarbonyl.

5. A pharmaceutical composition according to claim 1, characterized in that the compound according to Formula (I) is selected from the group of :
   - {4-[4-(1-Benzoyl-piperidin-4-yl)-piperazin-1-yl]-2-benzyl-piperidin-1-yl}-(3,5-bis-trifluoromethyl-phenyl)-methanone and
   - (2-Benzyl-4-{4-[1-(4-methyl-[1,2,3]thiadiazole-5-carbonyl)-piperidin-4-yl]-piperazin-1-yl}-piperidin-1-yl)-(3,5-bis-trifluoromethyl-phenyl)-methanone.

6. A pharmaceutical composition according to claim 1, characterized in that the compound according to Formula (I) is a compound with compound number 5, 110, 97, 45, 22, 151, 80, 62, 104, 8, 78, 12, 39, 113, 16, 56, 143, 36, 77, 106, 102, 6, 3, 142, 51, 9, 13, 32, 139, 4, 108, 89, 116, 2, 42, 140, 85, 37, 65, 133, 79, 64, 7, 141, 132, 134, 119, 90, 11, 26, 10 and 144 as cited in the Experimental section.

7. A pharmaceutical composition according to any one of claims 1 to 6, characterized in that it is formulated for simultaneous, separate or sequential use.

8. A pharmaceutical composition according to any one of claims 1 to 7, characterized in that the opioid analgesic is one or more compounds selected from the group of alfentanil, buprenorphine, butorphanol, carfentanil, codeine, diacetylmorphine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol, lofentanil, meperidine, methadone, morphine, nalbuphine, oxycodone, oxymorphone, pentazocine, propoxyphene, remifentanil and sufentanil; or a pharmaceutical acceptable salt or derivative thereof.

9. A pharmaceutical composition according to claim 8, characterized in that the

opioid analgesic is one or more compounds selected from the group of oxycodone, codeine, morphine, fentanyl, buprenorphine, hydrocodone, hydromorphone and pharmaceutical acceptable salts and derivatives thereof.

10. A pharmaceutical composition according to claim 9, characterized in that the opioid analgesic is one or more compound selected from the group of morphine sulphate and fentanyl citrate.

11. A pharmaceutical composition according to any one of claims 1 to 10, characterized in that it is in a form suitable to be orally administered.

12. The use of a pharmaceutical composition according to any one of claims 1 to 11 for the manufacture of a medicament for the prevention and/or treatment of pain and/or nociception.

13. The use of a pharmaceutical composition according to any one of claims 1 to 11 for the manufacture of a medicament for the opioid-based prevention and/or treatment of acute and chronic pain, more in particular in inflammatory, post-operative, emergency room (ER), breakthrough, neuropathic and cancer pain treatments.

14. The use of a pharmaceutical composition according to any one of claims 1 to 11 for the manufacture of a medicament for the prevention and/or treatment of emesis in opioid-based treatments of pain.

15. The use of a pharmaceutical composition according to claim 14 for the manufacture of a medicament for the prevention and/or treatment of nausea and vomiting in opioid-based treatments of pain.

16. The use of an NK_1-receptor antagonist, in particular an NK_1-receptor antagonist according to Formula (I), the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof and prodrugs thereof, for the manufacture of a medicament for the prevention and/or treatment of respiratory depression in opioid-based treatments of pain.

17. The use of an NK_1-receptor antagonist, in particular an NK_1-receptor antagonist

according to Formula (I), the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof and prodrugs thereof, for the manufacture of a medicament for reducing and/or overcoming the tolerance observed with opioids in opioid-based treatments of pain.